
Nuclear Division

Content

- ▼ Replication and division of nuclei.
- ▼ Chromosome behaviour in mitosis.
- ▼ The need for reduction division in sexual reproduction.

Learning Outcomes

Candidates should be able to:

- explain how growth, repair and asexual reproduction in animals and plants can be brought about by mitosis.
- explain the need for the production of genetically identical cells.
- explain how cancer is the result of uncontrolled cell division, and list factors that can increase the chances of cancerous growth.
- describe, with the aid of diagrams, the behaviour of chromosomes during the mitotic cell cycle, and the associated behaviour of the nuclear envelope, cell membrane and centrioles. (Names of the main stages are expected.)
- explain what is meant by homologous pairs of chromosomes.
- explain the meaning of the terms haploid and diploid, and the need for a reduction division prior to fertilisation in sexual reproduction. (Details of meiosis are not expected.)

Learning Outcome (a)

NUCLEAR DIVISION by MITOSIS

New cells (daughter cells) are formed by cell division. In the case of single celled organisms this is called **binary fission**. Cell division is initiated by the nucleus, and nuclear division is the first visible sign of the process of cell division. The commonest form of nuclear division is that of **mitosis** in which two genetically identical daughter nuclei are formed. Mitosis occurs in the cell division seen in growth, repair, the replacement of cells which have a limited life span like our red blood cells and skin cells, and in asexual reproduction in many plants and lower animals. The development of a multicellular organism from a fertilised egg by mitosis, means that all the cells of the body are genetically identical to the fertilised egg. The development of an organism from the fertilised egg is the story of the controlled expression of genetic information, with only a small fraction of the genes being expressed in cells as they differentiate to form tissues specialised for specific (and limited) functions. In mature cells most of the DNA is inactive all of the time.

Asexual reproduction does not involve the fertilization of gametes, and as a result of mitosis produces offspring which are genetically identical to each other (**clones**). Many multicellular organisms, especially plants, can reproduce their entire bodies in this way, either from specialised structures eg. strawberry runners, or single celled spores.

◆ CHECKPOINT SUMMARY

- ◆ Mitosis is nuclear division in which two daughter nuclei with the same chromosome number as the parent nucleus are produced, typically diploid nuclei producing diploid daughter nuclei.
- ◆ The daughter nuclei are therefore genetically identical to the nucleus of the cell that produced them (except for any mutations that may occur).
- ◆ Mitotic cell division is seen in growth, repair and asexual reproduction.
- ◆ As a result of mitosis in the growth of an organism from the fertilised egg, all cells are genetically identical.
- ◆ Similarly, offspring of asexual reproduction lack genetic variation.

Learning Outcome (b)

The NEED for GENETICALLY IDENTICAL CELLS

The production of genetically identical cells in the growth and development of multicellular organisms allows certain cells to retain the ability to develop into any other if needed, for example stem cells in mammals can divide to form any of the different types of blood cell. In the asexual reproduction of organisms it allows for the rapid exploitation of optimal conditions, where any variation would be disadvantageous.

Learning Outcome (c)

CANCER and FACTORS that INCREASE its CHANCES

Cancer is the general name given to a diverse group of diseases which are characterised by unregulated cell division and the formation of tumours (large masses of cells which are abnormal in appearance and have arisen from a single precursor cell.)

Cancer is essentially a genetic disease in that it results from mutations in genes encoding proteins regulating the normal growth of cells and the cell cycle. There are three main types of gene which, if they acquire mutations, may result in transformation of a normal cell to a tumour cell.

Proto-oncogenes: in the normal cell, these genes encode for products that are involved in stimulating normal cell division, cancer might result from activation of one of these growth promoting proto-oncogenes.

Tumour suppressor genes: in the normal cell these genes encode for proteins which suppress cell growth. It is thought that many of these genes encode proteins which suppress DNA synthesis. Thus a mutation in one of these suppressor genes may result in production of a defective protein and loss of suppression of cell growth and division.

Genes regulating cell death (apoptosis): as well as strict regulation of cell division, the death of cells is also closely regulated. The body may wish to destroy cells in order that they can be replaced by newer ones, or at other times it may wish to destroy cells that are now no longer required, such as the breast tissue after the menopause. This programmed cell death is referred to as apoptosis. Disruption of the genes encoding proteins involved in apoptosis may cause cells to escape programmed cell death and continue to divide to form a tumour.

Factors which increase the risk of cancer

The genetic mutation or mutations that cause cancer may arise by chance. However, there are certain groups of people who are more at risk of acquiring these mutations and consequently cancer itself:

Familial (hereditary): certain mutant genes may be passed from one family member to the next. This form of inherited cancer is rare. Certainly more commonly, an **increased risk** of cancer is inherited. For example, a man whose mother has bowel cancer, is himself four times more likely to develop bowel cancer.

Environmental: certain chemicals damage DNA. A chemical that increases the risk of developing a cancer is referred to as a **carcinogen** or as being **carcinogenic**. Carcinogens are found in cigarette smoke and in low levels in some common foods and food additives. Radiation in the form of ultra violet light, gamma rays and X-rays is also carcinogenic. It damages DNA and malignant transformation is more likely. Environmental factors may also include certain viruses and other pathogens which have been linked to increased risk of cancer.

Learning Outcome (d)

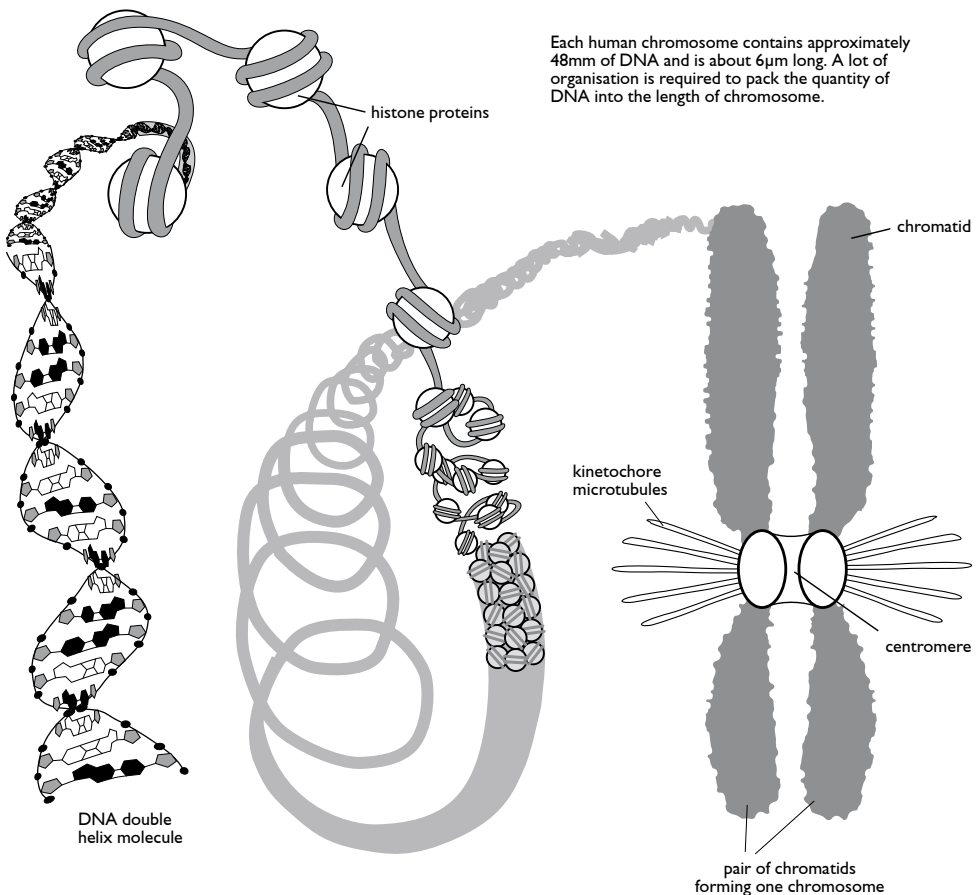
The MAIN STAGES of MITOSIS

Chromosomes only become visible when stained and viewed under the light microscope when the nucleus of a cell is just about to divide. This is because only at this time is the DNA/histone mixture wound up (condensed) as tightly as it can be. By this stage the DNA has also copied itself (replicated) so each chromosome appears double, and joined at one point (the **centromere**). Whilst they remain joined in this way the two daughter chromosomes are referred to as **chromatids**.

◆ CHECKPOINT SUMMARY

- ◆ Cancer is the result of uncontrolled mitotic cell division.
- ◆ Any factor that disrupts normal control of mitosis increases the chances of cancerous growth e.g. ultra-violet light, X-rays, and carcinogenic chemicals, e.g. tar, benzene.

Diagram showing how DNA is organised into a chromosome



Main stages of the mitotic cell cycle

Nuclear division (mitosis) occurs in four main stages, namely prophase, metaphase, anaphase and telophase.

Prophase is the first phase of mitosis, and as it begins, the DNA has already replicated, all protein synthesis has stopped, and each chromosome is condensed into the characteristic double chromatid, form. At the same time the cell rounds up, the nuclear membrane breaks down into small fragments, and a **spindle** of microtubules forms between two **microtubule organising centres (MTOCs)** at opposite poles of the cell.

Metaphase is defined as when the chromatids become attached to the spindle by structures called **kinetochores**. Kinetochores consist of microtubules and 'motor' proteins which utilise ATP energy to pull on the spindle. The effect of both sets of kinetochores pulling in opposite directions is that the chromosomes line up along the middle (equator) of the spindle.

Anaphase is defined when quite suddenly, and all at once, the chromatids of each pair separate, with each being pulled under tension in opposite directions towards the poles of the cell.

Telophase is the stage when the two new, identical sets of chromosomes reach the opposite poles and a new nuclear envelope forms to surround each set.

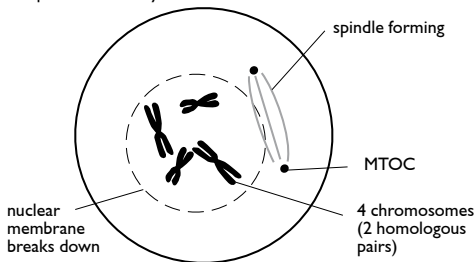
◆ CHECKPOINT SUMMARY

- ◆ The DNA replicates in interphase so that in the first stage of mitosis (prophase) the chromosomes appear as double structures of two chromatids (daughter chromosomes) joined at the centromere.
- ◆ The nuclear spindle apparatus(NSA) forms from the dissolution of the nuclear membrane and the centrioles replicate and migrate to either pole of the NSA.
- ◆ The centromeres align on the equator of the NSA (metaphase).
- ◆ The centromeres divide and the chromatids are moved to the opposite poles (anaphase).
- ◆ Two new daughter nuclei are formed (telophase).

Diagram to show stages in mitosis

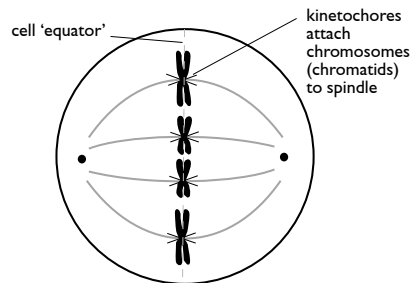
1 Prophase

Cell is rounded
MTOC's migrate to opposite poles
nuclear membrane disintegrates
spindle formed by MTOCs



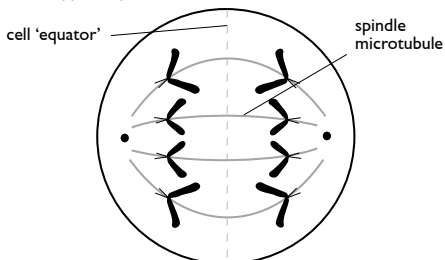
2 Metaphase

Chromosomes held on 'equator' of cell under tension. MTOCs at opposite poles



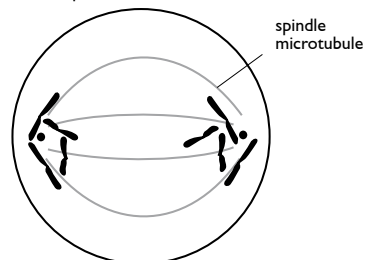
3 Anaphase

Chromatids separate and move towards opposite poles



4 Telophase

Beginnings of new nuclei at opposite poles
nuclear envelope reforms

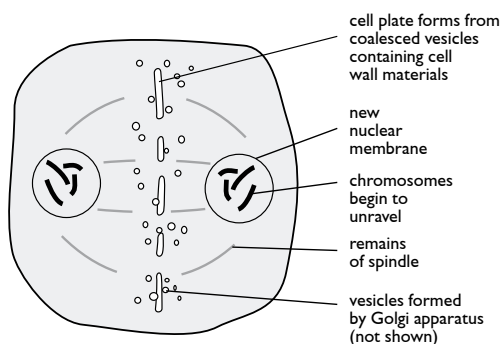


Nuclear division by mitosis is followed by division of the cytoplasm into two equal parts. This process is called **cytokinesis** and it occurs differently in animals and plants. In animal cells the spindle disintegrates during telophase and the microtubule components reassemble into a new cytoskeleton. The equator of the cell is constricted by a ring of contractile proteins (actin) in the process of cleavage, to create two roughly equal cells.

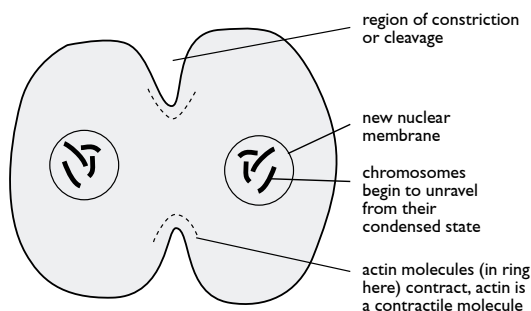
In plant cells the spindle lingers a little longer and seems to act as a guide to bring Golgi apparatus and associated secretory vesicles to the equator. The vesicles deposit their contents, which are the building constituents of a new cell wall, on the equator to form a plate of deposited material (the **cell plate**). Some of the vesicles remain intact and make connecting channels through the new cell wall (plasmodesmata).

Diagram showing the process of Cytokinesis

Cytokinesis in plant cells



Cytokinesis in animal cells



Interphase refers to the greater part of the life of a cell when there is no visible activity. The periods of mitosis and cytokinesis occupy only a fraction of the entire life of a cell. Together, interphase, mitosis and cytokinesis make up the **cell cycle**. The term interphase should not be interpreted to mean that the cell is resting. Interphase can itself be divided into three distinct periods called G1, S and G2. ('G' refers to the 'gaps' between DNA replication and mitosis.)

G1 is by far the longest period of the cell cycle. During G1, the cell machinery carries out protein synthesis, and growth occurs. All the cells of the body have identical sets of genes in their nuclei but the cells develop in different ways to perform different functions. This development process is called cell **differentiation** in which different genes are switched on and off so that only one small part of the genetic code is active in each cell.

After a period of growth and differentiation, the length of which depends upon a variety of internal and external factors, protein synthesis is suspended, and the DNA set replicates itself. This is the **S** phase. DNA replication is followed by another 'gap' period, **G2**, before mitosis starts, in which the cytoskeleton of the cell breaks down and the microtubule components begin to reassemble into spindle parts. Without a cytoskeleton, the cell assumes a more spherical shape (see prophase).

The timing of events within the cell cycle is extremely variable. In ideal conditions, where food and oxygen are in plentiful supply and temperature and pH values are optimal, bacterial cells can complete the cycle to produce a new generation every 20 minutes. Other cells, for example muscle cells, never complete the cycle and remain stuck in G2 until they die, a condition called **terminal differentiation**.

It has become clear that the onset of the S (DNA replication) phase and the M (mitotic) phase are determined by genes which are very similar in all organisms. These genes direct the synthesis of enzymes which in turn activate the enzymes initiating S and M phases.

The rate of cell division can be controlled by naturally occurring plant substances which affect the process of nuclear spindle formation. These include **vincristine** and **vinblastine** (from the periwinkle plant *Catharanthus rosea*). Both of these substances are used to control cancers such as leukaemia and lymphoma. They work, at a molecular level, by binding on to the spindle microtubules, preventing spindle assembly.

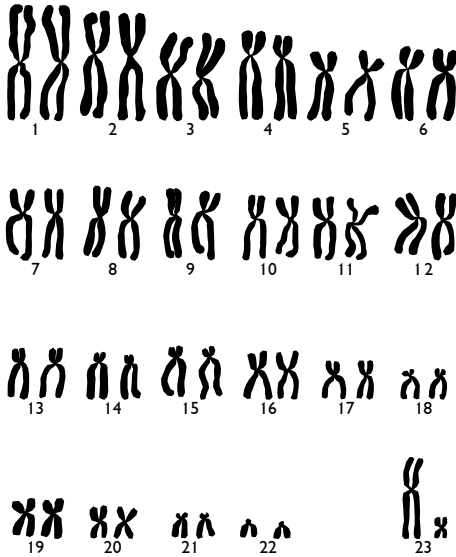
The plant substance, **taxol**, from the Pacific Yew (*Taxus brevifolia*) has almost the reverse effect on spindle formation, causing an over production of microtubules which effectively stops cell division. Taxol has been used to treat ovarian cancers.

Learning Outcome (e)

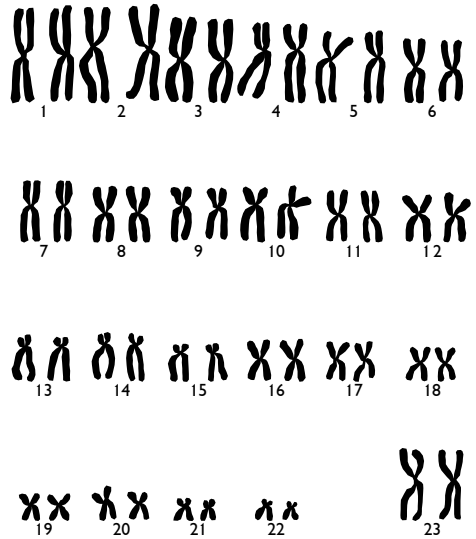
HOMOLOGOUS PAIRS of CHROMOSOMES

The DNA in eukaryotic cells is combined with **special nuclear proteins (histones)** to form 46 separate chromosomes. These 46 chromosomes constitute what is called the human **karyotype**. The 46 chromosomes exist as two sets of 23 chromosomes, one set of which is inherited from the mother's egg, and the other set from the father's sperm. The chromosomes of a pair have the same shape and structure and carry copies of the same genes (albeit often in a slightly modified form or **allele**). The chromosomes of a pair are said to be **homologous**. The sex chromosomes (X and Y chromosomes) are only partially homologous and carry different genes on their non-homologous 'arms', e.g. the Y chromosome carries male determining genes which are not found on the X chromosome.

Karyotype normal human male



Karyotype normal human female



Learning Outcome (f)

NEED for REDUCTION DIVISION PRIOR to FERTILISATION in SEXUAL REPRODUCTION

The only cells in the body which do not possess the double (**diploid**) set of homologous chromosomes are the gametes, which are **haploid**, meaning they only contain one of each pair. The nuclear division that produces haploid gametes is called **meiosis** which you will study later in the course. (Note the abbreviations, $2n$ = diploid, n = haploid)

The cell cycle

